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By: Patricia Andrus

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

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Application No.: 10/672,266

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For: LYOPHILIZED BEADS  
CONTAINING MANNITOL

Confirmation No. 8805

Examiner: Pande, Suchira

Technology Center/Art Unit: 1637

COMMUNICATION IN RESPONSE TO  
NOTICE OF NON-COMPLIANT APPEAL  
BRIEF

Mail Stop Appeal Brief  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Commissioner:

In response to the Notice of Non-Compliant Appeal Brief mailed June 8, 2009,  
Applicants provide the following replacement sections for the Appeal Brief mailed May 6, 2009:

3. Status of Claims beginning on page 2.
4. Status of Amendments beginning on page 2.
9. Claims Appendix beginning on page 3.

Remarks begin on page 13 of this paper.

### **3. STATUS OF CLAIMS**

Claims 1-10, 12, 45-48, 50-53, 63 and 64 are pending and appealed. Claims 11, 13-44, 49 and 54-62 are withdrawn from further consideration as being directed to a non-elected invention.

Claims 1-10, 12, 45-48 and 50-53 were rejected under 35 U.S.C. § 112, 1<sup>st</sup> and are appealed.

Claims 1-7, 10, 12, 45-48, 50, 52, 53, 63 and 64 were rejected under 35 U.S.C. § 103(a) and are appealed.

Claims 8 and 50 were rejected under 35 U.S.C. § 103(a) and are appealed.

Claims 9 and 51 were rejected under 35 U.S.C. § 103(a) and are appealed.

Independent claims 1, 45, 63 and 64, and dependent claims 2-10, 12, 46-48 and 50-53 are grouped together.

### **4. STATUS OF AMENDMENTS**

In accordance with 37 C.F.R. §41.37(c)(1)(viii) a copy of the claims involved in the appeal are contained in the Appendix attached hereto.

## **9. CLAIMS APPENDIX**

**1. (Previously Presented):** A lyophilized bead suitable for use in the amplification of a nucleic acid sequence, said lyophilized bead being substantially spherical in shape and comprising:

a thermally stable enzyme; and

mannitol;

wherein said lyophilized bead has a weight percentage of said mannitol of between about 53% and about 75% (w/w).

**2. (original):** The lyophilized bead of claim 1, wherein said amplification occurs in a reaction mixture comprising a volume of between about 5  $\mu$ L and about 200  $\mu$ L.

**3. (original):** The lyophilized bead of claim 1, further comprising a nucleoside triphosphate or a derivative thereof.

**4. (original):** The lyophilized bead of claim 1, wherein said lyophilized bead has an average cross-section of between about 1 millimeter and about 4.5 millimeters.

**5. (original):** The lyophilized bead of claim 1, wherein said weight percentage is between about 62% and about 75% (w/w).

**6. (original):** The lyophilized bead of claim 5, wherein said weight percentage is between about 68% and about 75% (w/w).

**7. (original):** The lyophilized bead of claim 1, wherein said thermally stable enzyme is selected from the group consisting of polymerase, ligase, and combinations thereof.

**8. (previously presented):** The lyophilized bead of claim 1, further comprising a component selected from the group consisting of an antibody that inactivates a polymerase and a wax or oil to sequester magnesium.

**9. (Previously Presented):** The lyophilized bead of claim 1, further comprising N-(2-Hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid) (HEPES).

**10. (original):** The lyophilized bead of claim 1, further comprising a probe.

**11. (withdrawn):** The lyophilized bead of claim 1, further comprising a reverse transcriptase.

**12. (original):** The lyophilized bead of claim 1, further comprising an internal control.

**13. (withdrawn):** A lyophilized bead suitable for use in the amplification of a nucleic acid sequence, said lyophilized bead comprising:

a forward polynucleotide primer;

a reverse polynucleotide primer; and

mannitol;

wherein said lyophilized bead has a weight percentage of said mannitol of between about 53% and about 75% (w/w).

**14. (withdrawn):** The lyophilized bead of claim 13, wherein said amplification occurs in a reaction mixture comprising a volume of between about 5  $\mu$ L and about 200  $\mu$ L.

**15. (withdrawn):** The lyophilized bead of claim 13, wherein said lyophilized bead has an average cross-section of between about 1 millimeter and about 4.5 millimeters.

**16. (withdrawn):** The lyophilized bead of claim 13, wherein said weight percentage is between about 62% and about 75% (w/w).

**17. (withdrawn):** The lyophilized bead of claim 16, wherein said weight percentage is between about 68% and about 75% (w/w).

**18. (withdrawn):** The lyophilized bead of claim 13, further comprising HEPES.

**19. (withdrawn):** The lyophilized bead of claim 13, further comprising a probe.

**20. (withdrawn):** The lyophilized bead of claim 13, further comprising an internal control.

**21. (withdrawn):** The lyophilized bead of claim 13, wherein said nucleic acid sequence is selected from the group consisting of bacterial, fungal, and viral nucleic acid sequences.

**22. (withdrawn):** The lyophilized bead of claim 21, wherein said bacterial nucleic acid sequence is derived from a member selected from the group consisting of *Bacillus Anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Francisella tularensis*, Group B *Streptococcus*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Xylella fastidiosa*.

**23. (withdrawn):** The lyophilized bead of claim 21, wherein said viral nucleic acid sequence is derived from a member selected from the group consisting of Vaccinia, West Nile Fever virus, Equine Encephalitis virus, and Foot and Mouth Disease virus.

**24. (withdrawn):** A method for the amplification of a nucleic acid sequence, said method comprising:

(a) dissolving a lyophilized bead in a liquid, wherein said lyophilized bead comprises:

a thermally stable enzyme; and  
mannitol;

wherein said lyophilized bead has a weight percentage of said mannitol of between  
about 53% and about 75% (w/w), thus forming a reaction mixture; and

(b) subjecting said reaction mixture to an amplification reaction.

**25. (withdrawn):** The method of claim 24, wherein said reaction mixture further  
comprises a volume of between about 5  $\mu$ L and about 200  $\mu$ L.

**26. (withdrawn):** The method of claim 24, wherein said reaction mixture further  
comprises a nucleoside triphosphate or a derivative thereof.

**27. (withdrawn):** The method of claim 24, wherein said thermally stable enzyme is  
selected from the group consisting of polymerase, ligase, and combinations thereof.

**28. (withdrawn):** The method of claim 24, wherein said reaction mixture further  
comprises a forward polynucleotide primer.

**29. (withdrawn):** The method of claim 24, wherein said reaction mixture further  
comprises a reverse polynucleotide primer.

**30. (withdrawn):** The method of claim 24, wherein said reaction mixture further  
comprises a probe.

**31. (withdrawn):** The method of claim 24, wherein said reaction mixture further  
comprises a nucleic acid comprising said nucleic acid sequence.

**32. (withdrawn):** The method of claim 24, wherein said reaction mixture further  
comprises HEPES.

**33. (withdrawn):** The method of claim 24, wherein said reaction mixture further comprises an internal control.

**34. (withdrawn):** The method of claim 24, wherein said reaction mixture further comprises a hot start methodology.

**35. (withdrawn):** The method of claim 24, wherein said lyophilized bead has an average cross-section of between about 1 millimeter and about 4.5 millimeters.

**36. (withdrawn):** A method for the amplification of a nucleic acid sequence, said method comprising:

(a) dissolving a lyophilized bead in a liquid, wherein said lyophilized bead comprises:

a forward polynucleotide primer;  
a reverse polynucleotide primer; and  
mannitol; and

wherein said lyophilized bead has a weight percentage of said mannitol of between about 53% and about 75% (w/w), thus forming a reaction mixture; and

(b) subjecting said reaction mixture to an amplification reaction.

**37. (withdrawn):** The method of claim 36, wherein said reaction mixture further comprises a volume of between about 5  $\mu$ L and about 200  $\mu$ L.

**38. (withdrawn):** The method of claim 36, wherein said reaction mixture further comprises a nucleoside triphosphate or a derivative thereof.

**39. (withdrawn):** The method of claim 36, wherein said reaction mixture further comprises a probe.

**40. (withdrawn):** The method of claim 36, wherein said reaction mixture further comprises a nucleic acid comprising said nucleic acid sequence.

**41. (withdrawn):** The method of claim 36, wherein said reaction mixture further comprises HEPES.

**42. (withdrawn):** The method of claim 36, wherein said reaction mixture further comprises a thermally stable enzyme.

**43. (withdrawn):** The method of claim 36, wherein said reaction mixture further comprises an internal control.

**44. (withdrawn):** The method of claim 36, wherein said lyophilized bead has an average cross-section of between about 1 millimeter and about 4.5 millimeters.

**45. (Previously Presented):** A lyophilized bead suitable for use in the amplification of a nucleic acid sequence, said lyophilized bead being substantially spherical and prepared by a process comprising:

(a) creating an aqueous solution, said aqueous solution comprising:

a thermally stable enzyme; and  
mannitol;

wherein said solution has a concentration of said mannitol between about 0.38 M (moles of mannitol/liter of solution) and about 0.99 M (moles of mannitol/liter of solution);

(b) quick-freezing the product of (a); and

(c) freeze-drying the product of (b).

**46. (original):** The lyophilized bead of claim **45**, wherein the product of (c) has an average cross-section of between about 1 millimeter and about 4.5 millimeters.

**47. (original):** The lyophilized bead of claim **45**, wherein the product of (c) further comprises a nucleoside triphosphate or a derivative thereof.

**48. (original):** The lyophilized bead of claim **45**, wherein said thermally stable enzyme is selected from the group consisting of polymerase, ligase, and combinations thereof.

**49. (withdrawn):** The lyophilized bead of claim **45**, wherein the product of (c) further comprises a reverse transcriptase.

**50. (previously presented):** The lyophilized bead of claim **45**, wherein the product of (c) further comprises a component selected from the group consisting of an antibody that inactivates a polymerase and a wax or oil to sequester magnesium.

**51. (Previously Presented):** The lyophilized bead of claim **45**, wherein the product of (c) further comprises N-(2-Hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid) (HEPES).

**52. (original):** The lyophilized bead of claim **45**, wherein the product of (c) further comprises a probe.

**53. (original):** The lyophilized bead of claim **45**, wherein the product of (c) further comprises an internal control.

**54. (withdrawn):** A lyophilized bead suitable for use in the amplification of a nucleic acid sequence, prepared by a process comprising:

(a) creating an aqueous solution, said aqueous solution comprising:

a forward polynucleotide primer;  
a reverse polynucleotide primer; and  
mannitol;

wherein said solution has a concentration of said mannitol between about 0.38 M (moles of mannitol/liter of solution) and about 0.99 M (moles of mannitol/liter of solution);

- (b) quick-freezing the product of (a); and
- (c) freeze-drying the product of (b).

**55. (withdrawn):** The lyophilized bead of claim 54, wherein the product of (c) has an average cross-section of between about 1 millimeter and about 4.5 millimeters.

**56. (withdrawn):** The lyophilized bead of claim 54, wherein the product of (c) further comprises a nucleoside triphosphate or a derivative thereof.

**57. (withdrawn):** The lyophilized bead of claim 54, wherein the product of (c) further comprises HEPES.

**58. (withdrawn):** The lyophilized bead of claim 54, wherein the product of (c) further comprises a probe.

**59. (withdrawn):** The lyophilized bead of claim 54, wherein the product of (c) further comprises an internal control.

**60. (withdrawn):** A lyophilized bead suitable for use in microanalytic systems comprising:

a moisture-sensitive reactant; and

mannitol;

wherein said lyophilized bead has a weight percentage of said mannitol of between

about 53% and about 75% (w/w); and

wherein said lyophilized bead has an average cross-section of between about 1

millimeter and about 4.5 millimeters.

**61. (withdrawn):** The lyophilized bead of claim 60, wherein said weight percentage is between about 62% and about 75% (w/w).

**62. (withdrawn):** The lyophilized bead of claim 60, wherein said weight percentage is between about 68% and about 75% (w/w).

**63. (Previously Presented):** A lyophilized bead suitable for use in the amplification of a nucleic acid sequence, said lyophilized bead comprising:

a thermally stable enzyme; and

mannitol;

wherein said lyophilized bead has a weight percentage of said mannitol of between about 53% and about 75% (w/w).

**64. (Previously Presented):** A lyophilized bead suitable for use in the amplification of a nucleic acid sequence, prepared by a process comprising:

(a) creating an aqueous solution, said aqueous solution comprising:

a thermally stable enzyme; and

mannitol;

wherein said solution has a concentration of said mannitol between about 0.38

M (moles of mannitol/liter of solution) and about 0.99 M (moles of

mannitol/liter of solution);

(b) quick-freezing the product of (a); and

(c) freeze-drying the product of (b).

**REMARKS**

Applicants submit this communication in response to the Notice of Non-Compliant Appeal Brief of June 8, 2009. The Notice provided that section 3. Status of the Claims, did not identify the appealed claims. The appealed claims have now been identified. The Notice also provided that section 9. Claim Appendix did not provide a clean set of claims. Applicants note a clean set of claims is now provided in section 9. Section 4. Status of Amendments has also been updated to reflect the clean set of claims in section 9.

**CONCLUSION**

Applicants respectfully request entry of the instant communication and consideration of the instant Appeal.

Respectfully submitted,



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